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Physical activities, exercises, and their effects to the immune system

Titis Nurmasitoh.[1]

[1]Departmen of Physiology, Islamic University of Indonesia

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***Corresponding author:**
dr.putrya@gmail.com

ABSTRACT

Every systems in human body correlate to maintain homeostasis. One of those systems which contribute to maintain homeostasis is the immune system. The immune system defends physiological functions against foreign substances and cancer cells through a complex and multilayered mechanism. The ability to defend against foreign substances and abnormal cells is done by two types of immune system, which are Innate immune system and adaptive/acquired immune system. There are also certain factors that affect the immune system, for instance physiological factor, nutrition, psychological factor, environental factor, and exercise or physical activities. Regular exercises and physical activities with moderate intensity will boost the immune system. Sedentary lifestyle and minimal physical activity will increase the risk of infectious diseases. While exercises and physical activity with high intensity will suppress the immune system hence increase the risk of infection.

Sistem-sistem dalam tubuh manusia bekerja sama untuk mempertahankan homeostasis. Salah satu sistem yang berkontribusi mempertahankan homeostasis adalah sistem imun. Sistem imun mempertahankan fungsi tubuh terhadap invasi sel asing dan sel kanker melalui mekanisme pertahanan yang kompleks dan berlapis-lapis. Kemampuan untuk mengatasi substansi asing dan sel abnormal yang membahayakan dilakukan oleh kerja sama dua tipe sistem imun, yaitu sistem imun non-spesifik atau innate immune system *dan sistem imun spesifik atau* adaptive/acquires immune system*. Terdapat faktor-faktor tertentu yang mempengaruhi status imun, antara lain faktor fisiologis, nutrisi, psikologis, lingkungan, dan kebiasaan berolah raga atau beraktivitas fisik. Olah raga dan aktivitas fisik dengan intensitas moderat secara teratur akan meningkatkan sistem imun. Kebiasaan hidup sedenterian dan aktivitas fisik yang minimal akan meningkatkan risiko terkena penyakit infeksi. Selain itu, olah raga dengan intensitas berat dan sangat berat justru menekan sistem imun sehingga meningkatkan risiko terkena infeksi*

INTRODUCTION

Every systems in human body correlate to maintain homeostasis. All these systems support and compensate each other in order to maintain an optimal condition within the human body. One of these systems is the immune system. During all of our activities, our body is constantly in contact with external agents which might be harmful to us. For examples, include the entrance of any disease-causing microorganism into our body (virus, bacterias, parasites, etc), exposure to UV light from the sun, chemical poisons, physical or emotional stress, and so on. Eventhough human body is constantly exposed to both external and internal agents, we do not experience diseases or disturbance on a daily basis. In fact, most of us will maintain a healthy condition and only a small portion will develop illness.[1] This is possible because human body has a lot of systems which maintain homeostasis, one of which is defending against harmful external and internal agents. The immune system defends physiological functions

against foreign substances and cancer cells through a complex and multilayered mechanism. This defense is necessary in order to maintain the optimal function of the cells.[2]

One of a few factor that affect the immune system is physical activity and exercise. A lot of researches have shown correlation between physical activity and exercises toward physiological changes of the immune system. Although, the effect of physical activity and exercises toward the immune system and its consequence to the risk of infection, is still being developed and researched.[3-6] This article will discuss the effect of physical activity and exercise towards the immune system. A short summary about the immune system and its mechanism, a short summary about physical activity and exercise, and the correlation between them will be discussed systematically.

THE PHYSIOLOGY OF IMMUNE SYSTEM

The immune system protects and eliminates foreign substances and abnormal cells that are harmful to the human body. The ability to defend and neutralize external or internal harmful exposures is called immunity. The immune system consist of cells, molecules, and tissues that are working together to defend against foreign substances and abnormal cells. This coordination and reaction in the immune system, which fight invasions or attacks of foreign substances, is called 'immune response.[7-8]

The ability to defend against foreign substances and abnormal cells is done by two types of immune system, which are Innate immune system and adaptive/acquired immune system. Human body has the innate immune system since birth. It consist of physical barrier (skin and mucous membrane), cellular component (natural killer cells or NK cells, and phagocytic cells, like neutrophils and macrophages), complement system, and various other substances that are produced by the innate immune system. Skin and mucous membrane are the first barrier that block the invasion of foreign substances. The epithelial cells of the mucous membrane secrete. Mucus is used to lubricate and moisturize its surrounding. Due to its thick consistency, mucus is able to inhibit and block the invasion of foreign substances that are trying to enter human body from the mucous membrane. Certain mucous membranes have hairs (nasal mucous membrane) and cilia (upper respiratory tract mucous membrane) which also block the entrance of foreign substances. Different types of liquids are also produced by the tissues around the mucous membrane, for instance : tears (contain lysozyme), saliva, gastric acid, and vaginal fluid. These liquids not only block the entrance of foreign substances, but also eliminate microbes and bacteria.[2,7]

Pathogen and foreign substances that manage to escape the first barrier will be faced with the second barrier which is part of the innate immune system cellular component. The cellular component of the innate immune system includes phagocytic cells and NK cells. Phagocytic cells will phagocytes (swallow) foreign substances like bacteria. Two important example of phagocytic cells are macrophages and neutrophils.

Neutrophil is an important phagocytic cell of the innate immune system because not only it destroys invading bacteria, an activated neutrophil will release chemical substances that will induce increasing blood flow to the area of infection. Neutrophil also produces cytokines that will activate the other cells of the immune system. Cytokines will send signal and regulate the communication between these cells. Cytokines will also act as a chemoatractan which will signal other cells of the immune system about the ongoing infection and attract these cells to the site of infections. Cytokines also contribute to other kind of immune response, such as : inflammatory process, fever, or stimulate the production of other cells in the immune system.[9,10]

Macrophage, another type of phagocytic cells, works in a similar nature with neutrophils. Macrophage will directly identify, attach, form vesicles, and swallow the invading bacteria. Inside the macrophage, bacteria will be eliminated using the chemical properties of the macrophage. In addition to that, the chemical substances released by the macrophage during this process will increase blood flow to the site of infection. Increased blood flow will attract more leukocytes to the site of infection, hence contribute to the elimination of bacteria.

Besides that, macrophage also releases cytokines which will act as chemoattractan. Other types of white blood cells, like basophils and eosinophils, are also a part of the innate imune system.[9,11]

Meanwhile, the NK cells act as a multipurposed cell of the innate immune system. When activated, NK cells will attack many kind of pathogen, including bacteria, parasytes, fungi, and cancerous cells. It also releases cytokines. The complement system of the innate immune system contributes in eliminating pathogen by forming membrane attack complex (MAC), assisting other cells of the immune system to activate and recognize the pathogen more easily. And it also acts as a chemoattractan.[5,9,10]

Human body is also equipped with adaptive/acquired immune system which has a memory that will recognize and remember many kinds of pathogens and form a spesific immunity against them. Due to this ability, once another invasion of previous pathogen occur, the adaptive/acquired immune system will be able to respond better and eliminate the pathogen. It also has the ability to remember and adapt against previous pathogens, as well as preparing itself for the next attack. Major components of the adaptive/acquired immune system are B lymphocytes and T lymphocytes.[2,8,9]

B lymphocytes contribute to the immune system mainly by secreting antibodies or immunoglobulins (Ig). There are five known antibody, which are IgG, IgM, IgA, IgD, and IgE. When B lymphocytes are activated by an invasive antigen, Immunoglobulin M (IgM) will be the first to be produced. Ig M protects the body from pathogen using two mechanisms. First, IgM activates the complement cascade. Immunoglobulin that merges with other proteins, in this case—complement proteins, will react better against antigens. Second, IgM will neutralize virus by binding it so that it can not infect surrounding cells. On the other hand, IgG is an important and dominant immunoglobulin in our body. Binding between IgG and antigen, whether virus or bacteria, will activate other cells of the immune system, such as macrophage, neutrophils, and NK cells.[9,10]

T lymphocytes has three main types, which are T cytotoxic, T helper, and T regulator. T cytotoxic identify and eliminates invading viruses. T helper, assist the process of other immunologic cells by secreting cytokines. T helper also facilitate other immunologic cells to initiate acquired/adaptive immune system. While, T regulator, regulates the functions and responses of acquired/adaptive immune system.[5,9,11]

Many researches shows that there are multiple factors which affect immune status. These factors will affect the risk of infections and diseases. One of these factors is physiological factor, for example aging. Physiologically, immune system will decline once someone enters their 50th of age.[12] Other factors include diet and nutritions. Many researches about nutritional substances that boost the immune system are currently widely researched.[13] Psychological factor is also known to affect the immune system. A researched that was done to patients with insomnia showed impairment in the functions of various cells of the immune system. Psychological stress also alterred the immune system and caused immunosupression effect. This was caused by the increase of cortisol concentration in the circulation.[11,14] Other factors that affect the immune system include environmental factor, as well as physical activities and exercises.[14]

PHYSICAL ACTIVITIES AND EXERCISES

Since ancient Greece, people has believed that exercise would boost someone's health. The development of science about exercise was drastically seen during the 19th century, especially in various university of the Great Britain. At that time, health was not the main goal of physical exercises. Beneficial properties that widely promoted was its effect on moral conformation—coherent with the saying "a sound mind in a sound body". Even until now, exercise is becoming more and more important in health promotion, especially in industrial countries across the world.[15] Besides that, the correlation between regular exercise and mental health is making a comeback to the trend. This is marked by an increased of popularity of exercises like Yoga.

Generally, physical activities is believed to have positive effects on human body. This is also supported by various researches. Physical activity is proven to influence the balance of energy and bodily composition. Physical activities and exercises are also currently being developed to ease post-operative complains, as

well as for patients in recovery period or chronic depression. In addition to that, physical activity is a modifiable factor and, more importantly, protective factor in cardiovascular diseases, stroke, hypertension, type 2 diabetes mellitus, osteoporosis, colon and breast cancer, and other chronic degenerative diseases. Hence, regular physical activity will reduce the risk of those diseases.[15-17] The term 'Physical activity' is often being merged with 'Exercises', while in fact, these terms have different meaning. Physical activity is defined as any movement of the body, caused by the activity of sceletal muscle and causing an increase of energy consumption. Physical activity includes daily activity (such as : taking care of children or doing house chores), moving places (such as : walking or cycling somewhere), and leisure activities (such as : dancing or swimming). This term also includes all forms of bodily movement in term of competitive sports, leisure sports, and daily activities.[6,16,18] In the other hand, 'exercise' is defined as structured, planned, and repetitive physical activities that aim to acquire or improve one or more components of fitness. Therefore, exercises can be viewed as a subcategory of physical activity. Nevertheless, both terms have a lot in common. Physical activity that stimulates the cardiorespiratory system, musculosceletal system, and metabolism will lead to more efficient performance and adaptation of the human body, hence improving fitness. Besides affecting the cardiorespiratory and other systems mentioned above, fitness also has more components, such as strength, flexibility, velocity, and optimal body fat.[6,16,19]

Exercises and physical activities are classified based on their frequency, duration, and intensity. Intensity measurement of physical activity is based on the amount of energy consumption during the activity which is measured in metabolic ecquivalents (METs=kcal/kg/minute).

Intensity also represent the amount of oxygen consumption during certain activity. One MET is an average measurement of a person's metabolism rate at rest, which is equivalent to 3,5 ml of oxygen consumption per kilogram body weight in 1 minute. Intensity of physical activity is categorized into : inactive, mild, moderate (3-6 METs), and high (> 6 METs).[6,15,16]

Another way to describe the intensity of physical activity is using the maximum percentage of oxygen consumption during a certain activity (VO2max). Due to strong correlation between oxygen consumption and pulse rate during physical activity, maximum percentage of pulse rate is often use to measure oxygen consumption. Maximum pulse rate based on the Karvonen formula is described as 220 minus age. According to ACSM (American College of Sport Medicine) recommendation, a person who is doing moderate intensity exercise should reach 55-70% of their maximum pulse rate during the exercise. While the standard for high intensity exercise is 70-90% of maximum pulse rate, very high is >90% of maximum pulse rate, sedentary is <40% of maximum pulse rate, and mild intensity is 40-55% of maximum pulse rate.[16,20,21]

Various researches have shown that moderate intensity exercises provide positive impact on health. It will reduce the risk of various chronic degenerative diseases and their mortality rate (Romeo et al., 2010). In certain chronic diseases, the success rate of exercise prescription in reducing the risk or treating the disease is very dependant on the individual dosing of each case. This individual dosage is mainly range in the moderate intesity.[15-17]

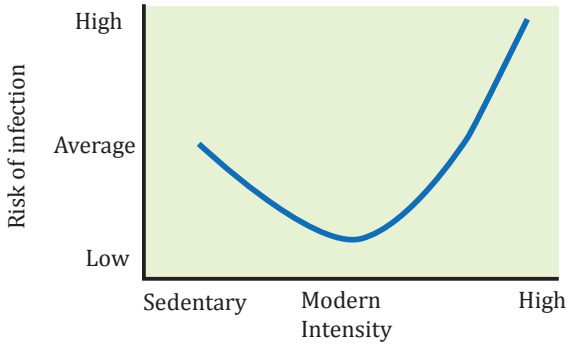
Exercise and physical activity is one of many factors that influence the immune system. However, its effect to the function of the immune system and the risk of infection is still an interesting and developing topic for researchers.

CORRELATION BETWEEN PHYSICAL ACTIVITY AND EXERCISE WITH THE IMMUNE SYSTEM

Physical activity and exercise is viewed as two sides of a coin. Its effect can either be positive (beneficial) or negative (disadvantageous). Likewise, its effect to the immune system. Nieman (1994) proposed a J-shaped curve which described the correlation between physical activity and exercise with the risk of upper respiratory tract infection (Picture 1). This curve was, then, widely known and used to describe

the relationship between physical activity and exercise with the immune system.[22]

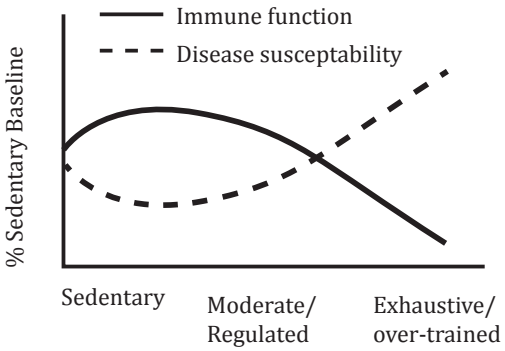
Based on the J-shaped curve, people who perform moderate exercises and physical activities has lower risk of developing upper respiratory tract infection compare to those who is inactive or perform low intensity physical activities and exercises. Moreover, they also has lower risk of developing upper respiratory tract infection compare to those who perform high intensity physical activities and exercises. This result showed that high intensity physical activites and exercises actually raised the risk of infection compare to moderate intensity physical activities.[3,10,22]



Picture 1 J-shaped curve [4,11]

A part of the J-shaped curve proposed by Nieman (1994), Woods et al. (1999) had also proposed a hypothesis about the reversed J-shaped curve (Picture 2). Reversed J-shaped curve is basically similar with the J-shaped curve. It explained that susceptibility of infection would increase in people with sedentary lifestyle and those who perform high intensity physical activities and exercises, compare to those who perform moderate physical activities and exercises. In addition to being affected by the intensity of physical activities and exercises, the reversed J-shaped curve also showed the influence of types and duration of the activities.[6,23]

Various researches has proven and support the concept of J-shaped curve. These researches showed that people who perform regular moderate exercises has lower risk of developing upper respiratory tract infection or flu, compare to those with sedentary lifestyle or perform high intensity and over-duration exercises. Examples of moderate intensity exercises is aerobic. Such as brisk walking, jogging, cycling, swimming, and rythmic gymnastic with regular moderate intensity. These exercises have protective influence to the immune system, but its mechanism is still being researched and developed. A few hypothesis regarding its mechanism has been proposed.[3,10,11]



Picture 2 Reversed J-shaped curve[6,23]

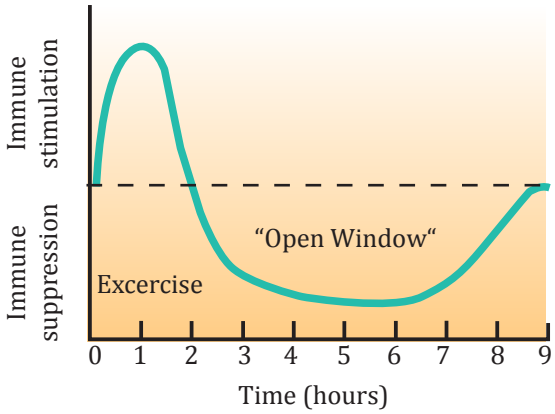
The first hypothesis proposed that moderate intensity exercises increase the amount of NK cells, neutrophils, and antibodies. Hence, it would improve the innate immune system acutely and gradually decreased back into its normal stage within 3 hours. Eventhough according to this theory exercises would only increase the innate immune system in a short period of time, it was thought to already give its protective effect and lower the risk of infections.[10,11,24]

Another mechanism of the protective effects of moderate-intensity exercise on the immune system related to positive effects of sport in the general body. People who are accustomed to moderate intensity exercise routine will improve psychological conditions, lowering the emotional stress, improve nutritional status, and improve the sleep habits. The positive effects of such sport will indirectly improve the immune system, also reducing the risk of infection.[11,14]

In the other hand, high intensity exercises or over-duration exercises will, contrary, increase the risk of infection. Various reports has been submitted by coaches and athletes in high intensity or over-duration sports. These reports mainly explained about the relationship between high intensity exercises with the increase risk of upper respiratory tract infection and influenza. In comparison with general population, athletes who perform high intensity exercises (ex :

marathon) has 2-6 times higher risk of developing sore throat and flu-like symptoms. Nevertheless, these reports does not necessarily explained causality between the two. A few theory was proposed to try to explain its mechanism. High intensity or over-duration exercises is thought to suppress the immune system. This is caused by the decreased of the amount and activity of B lymphocytes, T lymphocytes, and NK cells. Besides that, high intensity exercises will decrease the activity of phagocytic neutrophils, decrease the concentration of IgA, and increase the concentration of pro- and anti-inflammatory cytokines. Therefore, the activity of the immune system will be altered.[4]

People who perform high intensity exercises will experience a condition called "open window" (Picture 3). Open Window is defined as a condition where the immune system will undergo a depression state after an exercise. This will allow virus and bacteria to invade the human body, hence the risk of infection will be higher. The biological mechanism related to this event is presumed to be connected to the release of the stress hormones, Cortisol. A person who do high intensity exercise will have higher cortisol level in his circulation. Cortisol is known to have an immunosuppresive nature. It will inhibit the function of cytokines and NK cells, as well as reducing the production of T lymphocytes and altered its function.[5,10]



Picture 3 Curve of "open window" [5,10]

In addition to its relation to the Cortisol, suppresion of the immune system in high intensity exercises is also presumed to be related to the nature of the exercises. High intensity exercises are thought to cause less sleep or rest duration, increase mental stress, increase exposure to pathogen, the air condition during the exercise, and inadequate nutritional intake. These condition will impact the immune sistem negatively and increase the risk of infection.[11,14]

CONCLUSION

Every systems in human body correlate to maintain homeostasis, one of those systems is the immune system. Immune system consist of innate immune system (Physical barrier, NK cells, neutrophils, complement system) and adaptive/ acquired immune system (T lympocytes and B lymphocytes). One of a few factor that affect the immune system is physical activity and regular exercise. Regular exercises and physical activities with moderate intensity will boost the immune system. Sedentary lifestyle and minimal physical activity will increase the risk of infectious diseases. Exercises and physical activity with high intensity will suppress the immune system, hence increase the risk of infection.

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